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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,693	10/16/2003	Michael West	60141.0041USU1	6774

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/685,693	WEST ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-157* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-157* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-102, drawn to *ex vivo* methods of identifying genes and determining relative timing of transcriptional activation or repression of said genes in stem cells during differentiation, classified in class 435, subclass 6.

Two different species elections are required for Group I: marker DNA type and embryonic stem cell type.

Should Group I be elected, further species election is required: Claims 1-4, 6-9, 11-13, 15-18, 19-26, 60-67,69-91, 93-102 are generic to a plurality of disclosed patentably distinct species comprising a nucleotide sequence that encodes a protein selected from the group consisting of:

Ia. a fluorescent protein, as recited in claims 5, 10, 14, 68, 92

Ib. an enzyme that catalyzes production of a chromogenic or fluorescent product, as recited in claims 5, 10, 14, 68, 92

Ic. a protein that confers resistance to a selection agent, as recited in claims 5, 10, 14, 68, 92

Id. an intracellular antigenic protein, as recited in claims 5, 10, 68, 92

Ie. an antigenic cell surface protein that is exposed to a cell exterior, as recited in claims 5, 10, 14, 68, 92

If. a fusion protein, as recited in claims 14, 92

Applicant is required under 35 U.S.C. 121 to elect a single species of marker DNA (Ia-If), even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species are distinct, each from the other because of the following reasons: The marker DNA recited in species Ia, Ib, Ic, Id, Ie, and If, above, are directed to products that are functionally distinct and capable of separate use. Fluorescent proteins have the inherent characteristic of being able to absorb and emit light at certain wavelengths and have numerous uses, including incorporation into pet fish. Enzymes that catalyze reactions (including chromogenic or fluorescent products), are normally

responsible for the cleavage, joining, or transfer of chemical moieties. Proteins that confer resistance to a selection agent are capable of inactivating some toxic or static agent; a variety of mechanisms might confer this ability to the protein, including altering receptors, altering topoisomerases, or altering membrane transport proteins. Intracellular proteins by definition, exist inside the cell membrane, in a milieu quite different from that of the cell surface or extracellular environment. The nature and activities of proteins in this environment would be distinct from those integrated into the cell membrane. A fusion protein made from combinations of the proteins described above, would contain activities which are distinct from any one of the unique species.

Because these species are structurally distinct for the reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all of the subject matter being sought in the presently pending claims, and thus, restriction/species election for examination purposes as indicated is proper.

In addition to the species election of marker DNA, should Group I be elected, further species election is required: Claims 1-4, 6-9, 11-13, 15-18, 19-26, 60-67,69-91, 93-102 are generic to a plurality of disclosed patentably distinct species of embryonic stem cells selected from the group consisting of:

I-1. a murine embryonic stem cell or germ cell, as recited in claims 4, 22, 44, 61, 85;

I-2. a bovine embryonic stem cell or germ cell, as recited in claims 4, 22, 44, 61, 85;

I-3. a porcine embryonic stem cell or germ cell, as recited in claims 4, 22, 44, 61, 85;

I-4. a non-human primate embryonic stem cell or germ cell, as recited in claims 4, 22, 44, 61, 85;

I-5. a human embryonic stem cell or germ cell, as recited in claims 4, 22, 44, 61, 85;

Applicant is further required under 35 U.S.C. 121 to elect a single species of embryonic stem cell (I-1 through I-5), even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species are distinct, each from the other because of the following reasons: The embryonic stem cells recited in species I-1, I-2, I-3, I-4, and I-5, above, are directed to products that are functionally distinct and capable of separate use. Because embryonic stem (ES) cells differentiate along a species-specific pathway and are subtly affected by molecular and chemical signals, the changes in gene expression measured by Invention I would be applied only to the changes within each distinct species of embryonic stem cells. Although there are some conserved differentiation responses in all mammalian cells, there are also many species-specific differentiation responses to stimuli. The species are not used together. In addition, the nucleic acid and protein differences between homologous genes of different mammalian species guaranty that different reagents would be required for the tests involved in Invention I.

Because these species are structurally distinct for the reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all of the subject matter being sought in the presently pending claims, and thus, restriction/species election for examination purposes as indicated is proper.

II. Claims 18-59, drawn to *in vivo* methods of identifying genes and determining relative timing of transcriptional activation or repression of said genes in stem cells during differentiation, classified in class 435, subclass 6.

Two different species elections are required for Group II: marker DNA type and embryonic stem cell type.

Should Group II be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claims 18-20, 23-24, 27-39, 42-48, 50-59, 65-66, are generic to a plurality of disclosed patentably distinct species comprising a nucleotide sequence that encodes a protein selected from the group consisting of:

IIa. a fluorescent protein, as recited in claims 40, 49

IIb. an enzyme that catalyzes production of a chromogenic or fluorescent product, as recited in claims 40, 49

IIc. a protein that confers resistance to a selection agent, as recited in claims 40, 49

IId. an intracellular antigenic protein, as recited in claims 40, 49

IIe. an antigenic cell surface protein that is exposed to a cell exterior, as recited in claims 40, 49

In addition to the species election of marker DNA, should Group II be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claims 18-21, 23-43, 45-60, 62-66 are generic to a

plurality of disclosed patentably distinct species of embryonic stem cells selected from the group consisting of:

II-1. a murine embryonic stem cell or germ cell, as recited in claims 22, 44, 61;

II-2. a bovine embryonic stem cell or germ cell, as recited in claims 22, 44, 61;

II-3. a porcine embryonic stem cell or germ cell, as recited in claims 22, 44, 61;

II-4. a non-human primate embryonic stem cell or germ cell, as recited in claims 22, 44, 61;

II-5. a human embryonic stem cell or germ cell, as recited in claims 22, 61.

III. Claims 103-110, 128 drawn to a composition of isolated stem cells, classified in class 435, subclass 325.

Two different species elections are required for Group III: marker DNA type and embryonic stem cell type.

Should Group III be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claims 18-20, 23-24, 27-39, 42-48, 50-59, 65-66, are generic to a plurality of disclosed patentably distinct species comprising a nucleotide sequence that encodes a protein selected from the group consisting of:

IIIa. a fluorescent protein, as recited in claim 109;

IIIb. an enzyme that catalyzes production of a chromogenic or fluorescent product, as recited in claim 109;

IIIc. a protein that confers resistance to a selection agent, as recited in claim 109;

IIId. an intracellular antigenic protein, as recited in claim 109;

IIIe. an antigenic cell surface protein that is exposed to a cell exterior, as recited in claim 109.

In addition to the species election of marker DNA, should Group III be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claims 103-108 are generic to a plurality of disclosed patentably distinct species of embryonic stem cells selected from the group consisting of:

III-1. a murine embryonic stem cell or germ cell, as recited in claims 110;

III-2. a bovine embryonic stem cell or germ cell, as recited in claims 110;

III-3. a porcine embryonic stem cell or germ cell, as recited in claims 110;

III-4. a non-human primate embryonic stem cell or germ cell, as recited in claims 110;

III-5. a human embryonic stem cell or germ cell, as recited in claims 110;

IV. Claims 111-127 and 130-150, drawn to methods for determining conditions that induce stem cells to differentiate and methods of inducing a stem cell to differentiate into a particular cell type, classified in class 435, subclass 6.

Two different species elections are required for Group I: marker DNA type and embryonic stem cell type.

Should Group IV be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claim 111-114, 116-127, 130-138, and 140-150 are generic to a plurality of disclosed patentably distinct species comprising a nucleotide sequence that encodes a protein selected from the group consisting of:

IVa. a fluorescent protein, as recited in claims 115 & 139;

IVb. an enzyme that catalyzes production of a chromogenic or fluorescent product, as recited in claim 115 & 139;

IVc. a protein that confers resistance to a selection agent, as recited in claim 115 & 139;

IVd. an intracellular antigenic protein, as recited in claim 115 & 139;

IVe. an antigenic cell surface protein that is exposed to a cell exterior, as recited in claim 115 & 139;

IVf. a fusion protein, as recited in claim 139.

In addition to the species election of marker DNA, should Group IV be elected, further species election is required: The rationale for the distinctions between the species is the same as in Group I, above. Claims 111-113,115-127, 130-133, and 135-150 are generic to a plurality of disclosed patentably distinct species of embryonic stem cells selected from the group consisting of:

IV-1. a murine embryonic stem cell or germ cell, as recited in claims 114, 134;

IV-2. a bovine embryonic stem cell or germ cell, as recited in claims 114, 134;

IV-3. a porcine embryonic stem cell or germ cell, as recited in claims 114, 134;

IV-4. a non-human primate embryonic stem cell or germ cell, as recited in claims 114, 134;

IV-5. a human embryonic stem cell or germ cell, as recited in claims 114, 134.

Should Group IV be elected, further species election is required. Claims 130-141, 143-146, and 148-150 are generic to a plurality of disclosed patentably distinct species of promoters from the group consisting of:

IV-i. a constitutive promoter, as recited in claims 142, 150;

IV-ii. an inducible promoter, as recited in claims 142, 147, 150;

IV-iii. a developmental stage-specific promoter, as recited in claims 142, 147, 150;

IV-iv. a cell-type specific promoter, as recited in claims 142, 147, 150;

Applicant is further required under 35 U.S.C. 121 to elect a single species of promoter (IV-i through IV-iv), even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species are distinct, each from the other because of the following reasons: The embryonic stem cells recited in species IV-i, IV-ii, IV-iii, and IV-iv, above, are directed to products that are functionally distinct and capable of separate use. Constitutive promoters activate gene transcription continuously. Inducible promoters allow gene transcription after being exposed to a molecular agent or other introduced stimuli. Developmental stage-specific promoters permit gene transcription only during a certain stage of cell differentiation. Cell-type specific promoters allow gene transcription only in particular cells. Each of these promoters has functional and structural characteristics that makes their activity unique. The differences between these

promoters are due to their distinct DNA structures. This physical difference between the nucleic acid structures of the promoters qualifies each species as a structurally distinct chemical compound and they are therefore distinct from one another.

Because these species are structurally distinct for the reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all of the subject matter being sought in the presently pending claims, and thus, restriction/species election for examination purposes as indicated is proper.

V. Claims 129 & 136, drawn to a method for identifying cell-cell interactions that induce differentiation, classified in class 435, subclass 7.1.

VI. Claims 151-157, drawn to a method of producing antibodies, classified in class 424, subclass 130.1.

Invention Distinctions

2. The inventions are independent or distinct, each from the other because:

Inventions I and II are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are

either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, Invention I is directed to *ex vivo* methods of identifying genes and determining relative timing of transcriptional activation (or repression) of said genes in stem cells during differentiation and Invention II is directed to *in vivo* methods of identifying genes and determining relative timing of transcriptional activation (or repression) of said genes in stem cells during differentiation. While many of the steps and materials of these methods are shared, there is one extremely important difference between the inventions that causes them to be classified as distinct and requires that they be restricted; this important difference is that one invention is applied in whole living organisms while the other is applied to cells outside a living body. The cell culture environment of *ex vivo* methods requires media and a variety of chemical and biological additives that can support the life and differentiation of cells. However, the internal environment of a living organism is more complex than cell culture and introduces a multitude of other macromolecules and even entire organ systems which will interact with the introduced invention and its products. In fact, it is well known in all the biological arts that there are frequent discrepancies between *in vivo* and *ex vivo* models because of the complexity of whole organisms. The searches required for Inventions I and II would be non-overlapping because of the nature of the biological systems in which the gene constructions are placed. Therefore, restriction is required.

Groups I, II, and IV-VI are different methods. Methods of (1) identifying genes and determining relative timing of transcriptional activation or repression of said genes in stem cells during differentiation (inventions I & II), and (2) method of determining conditions that induce stem cells to differentiate and method of inducing a stem cell to differentiate into a particular cell type (invention IV), (3) method for identifying cell-cell interactions that induce differentiation (invention V) and (4) producing antibodies (invention VI) differ with respect to reagents, method steps, and endpoints. Each of the methods contains differences from the other that make them distinct and non-overlapping, (1) determining the relative timing of the change in the level of expression of the marker DNA construct that occurs in differentiating cells, and (2) culturing the stem cells in the presence of one or more combinations of chemical, biological, and physical agents, (3) screening methods to identify cell pairs and (4) using purified cells or an extract thereof as an immunogen to elicit production of an antibody that binds specifically to a differentiation antigen of the purified cells . The searches of these methods require distinct queries and would not overlap. Therefore the examiner would experience undue burden and restriction is required.

Invention III (stem cell products) is related as product and process of use to Inventions I-II, and IV-VI. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In

the instant case, Invention III describes isolated stem cells that have two or more differentiation specific markers wherein at least one marker DNA construct is inserted into an endogenous gene. Inventions I-II, and IV-VI utilize various stem cells that have insertions into endogenous genes. However, Invention III as claimed can be used in a materially different process of using that product such as to study the effect of knocking out genes. Consequently, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, or divergent subject matter, or the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Notice of Possible Rejoinder

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**
Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Response Requirement

4. Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Multiple Inventors

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Examiner Contact Information

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave Nguyen** can be reached on **571-272-0731**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott Long
Art Unit 1633

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER